UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TOMOHIRO TSUJI,
YUSUKE MORI,
TAKASHI SAKATA, and
YUKIO HAMAGUCHI

Appeal No. 2005-0543
Application No. 09/992,221

ON BRIEF

Before WILLIAM F. SMITH, ELLIS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134. Claims 1 and 11 are representative of the subject matter on appeal, and read as follows:

1. A method of classifying and counting leukocytic cells and erythroid cells in a bone marrow fluid comprising leukocytic cells and erythroid cells and lipid particles comprising the steps of:

   (1) (a) mixing a sample of the bone marrow fluid with an erythrocyte lysing agent to lyse erythrocytes in the sample, thereby rendering leukocytic cells, erythroid cells and lipid particles in the sample suitable for staining, and

(b) staining the sample with a fluorescent dye for producing a difference in intensity of fluorescence among the leukocytic cells, the erythroid cells, and the lipid particles;

(2) introducing the resulting sample to a flow cytometer to detect at least one kind of scattered light and at least one kind of fluorescence;

(3) classifying the lipid particles, the leukocytic cells and the erythroid cells by the difference in the intensities of their fluorescence and their scattered light; and

(4) obtaining a count of the leukocytic cells and erythroid cells in the step of (3).

11. A method of classifying and counting leukocytic cells and erythroid cells in a bone marrow fluid comprising leukocytic cells and erythroid cells and lipid particles comprising the steps of:

(1) (a) mixing a sample of the bone marrow fluid with an erythrocyte lysing agent to lyse erythrocytes in the sample, thereby rendering leukocytic cells, erythroid cells and lipid particles in the sample suitable for staining, and

(b) staining the sample with a fluorescent dye for producing a difference in intensity of fluorescence among the leukocytic cells, the erythroid cells, and the lipid particles;

(2) introducing the resulting sample to a flow cytometer to detect side scattered light and at least one kind of fluorescence;

(3) classifying the lipid particles, the leukocytic cells and the erythroid cells by the difference in the intensities of their fluorescence and their scattered light; and

(4) obtaining a count of the leukocytic cells and erythroid cells in the step of (3).

The examiner relies on the following references:

Hansen et al. (Hansen)	4,284,412	Aug. 18, 1981
Hoffman et al. (Hoffman)	4,492,752	Jan. 8, 1985
Inami et al. (Inami)	5,298,426	Mar. 29, 1994
Kim et al. (Kim '695)	5,516,695	May 14, 1996
Kim et al. (Kim '037)	5,559,037	Sep. 24, 1996

Bentley et al. (Bentley), "Correction of Bone Marrow Nucleated Cell Counts for the Presence of Fat Particles," American Journal of Clinical Pathology, Vol. 104, No. 1, pp. 60-64 (1995)

Claims 1-11 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Inami, Kim '037, Hansen, Hoffman, Bentley and Kim '695. After careful review of the record and consideration of the issue before us, we reverse.

DISCUSSION

In the rejection, Inami is cited for teaching a method for measuring erythrocytic nucleated cells, in which a sample of blood cells containing erythroblasts is mixed with a hypotonic lysis solution at a pH of 3.5 to 5, resulting in the lysis of the erythrocytes. See Examiner's Answer, page 4. A fluorescent nuclear dye is also added to differentially stain the nucleated cells, and the sample is subjected to flow cytometric analysis via scattered light and fluorescence, allowing the nucleated cells to be differentiated and counted. See id. The reference is also cited for teaching that the method may be applied to bone marrow samples. See id. Kim, Hansen and Hoffman are cited for teaching similar flow cytometric techniques.

According to the rejection:

> Inami, Kim '037, Hansen and Hoffman demonstrate that the claimed dyes were all known to the artisan of ordinary skill to be useful in the analysis of blood cell-containing samples, such as bone marrow, using the claimed analytical parameters of fluorescent and light scattering intensity, as recited in the claims under examination. Inami, Kim '037, Hansen and Hoffman differ from the claims under examination in that those patents fail to disclose the step of classifying the lipid particles present in the analyzed marrow sample as part of the step of analysis by fluorescence and scattered light.

Id. at 5-6.

Bentley is the relied upon for "establish[ing] the importance of classifying the fat particles in a bone marrow sample so that an accurate TNC can be obtained, by compensating for the amount of lipid particles in the sample." Id. at 6.

The rejection concludes:

> Thus, one of ordinary skill in the art performing the analytical procedures of Inami, Kim '037, Hansen and Hoffman would have been motivated by Bentley to have classified the lipid particles present in the marrow sample, and thereby obtain a more accurate cell count. It is proper to combine Inami, Kim '037, Hansen and Hoffman with Bentley, because all references are directed to solving the same problem—obtaining accurate TNC cell counts in blood cell-containing samples.

Id. at 6.

Appellants argue that "the examiner [has not] explained why the proposed modification of Bentley in view of any other cited references would have been desirable." Appeal Brief, page 8. We agree.

"A rejection based on section 103 clearly must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, all facts must be considered. The Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because it may doubt that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis. To the extent the Patent Office rulings are so supported, there is no basis for resolving doubts against their correctness. Likewise, we may not resolve doubts in favor of the Patent Office determination when there are deficiencies in the record as to the necessary factual bases supporting its legal conclusion of obviousness." In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968) (emphases in original).

The examiner, in the final rejection, stated that the fluorescent method of Inami, as well as Kim, Hansen and Hoffman was a "functional equivalent" of the absorbance method of Bentley. See Final Rejection mailed December 24, 2003. In the Examiner's Answer, however, the examiner states that

> Bentley is not cited for its use of any particular analytical technique per se. Rather, Bentley is cited for the fact that one practicing the cited art methods of cell counting and classification, such as disclosed by Inami [ ], would have recognized the desirability of classifying the lipid particles so as to ensure an accurate count of the total amount of cells present in the sample, as well as an accurate count of the various cell types therein. Thus, even assuming the techniques of Bentley would not have been considered equivalent to those of Inami and the other patents, the artisan of ordinary skill would nevertheless have recognized from

> Bentley the importance of classifying lipid particles in a marrow analysis, so as to ensure an accurate cell count, precisely as recited in appellants' claims.

Examiner's Answer, page 9.

Thus, as recognized by appellants, the examiner has changed his argument supporting the combination of Bentley with the other references. See Reply Brief, page 1. What the examiner has failed to provide, however, is a teaching or suggestion of why the ordinary artisan would look to Bentley, which uses an absorbance and impedence method, based on the Inami, Kim, Hansen and Hoffman references, which use fluorescent and scattered light. The rejection thus fails to set forth a prima facie case of obviousness, and based on the record before us, we are compelled to reverse it.

OTHER ISSUES

Bentley performs his marrow counts using a Cobias-Helios hematological analyzer. As seen from the abstract of Bentley et al., "Flow-cytochemical differential leukocyte analysis with quantitation of neutrophil left shift. An evaluation of the Cobas-Helios analyzer," Am. J. Clin. Path., Vol. 102, pp. 223-30 (1994), the Cobas-Helios analyzer classifies leukocytes by flow cytochemical techniques. In our review of the record we find no indication that either appellants or the examiner discuss the fact that Bentley is drawn to the use of flow cytometry for analyzing blood samples. Thus Bentley may in fact be the closest prior art and upon return of the application, the examiner may want to revisit the Bentley reference.

CONCLUSION

Because the examiner failed to set forth a prima facie case of obviousness, the rejection under 35 U.S.C. § 103(a) is reversed.

REVERSED

William F. Smith)
Administrative Patent Judge)
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Joan Ellis) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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) INTERFERENCES
)
Lora M. Green)
Administrative Patent Judge)

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Notice of References Cited	Application/Control No. 09/992,221	Applicant(s)/Patent Under Reexamination Appeal No. 2005-0543	
	Examiner BPAI	Art Unit	Page of

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
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	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
X	U	Bentley et al., "Flow-cytochemical differential leukocyte analysis with quantitation of neutrophil left shift. An evaluation of the Cobas-Helios analyzer." Am. J. Clin. Pathol., Vol. 102, No. 2 pp. 223-30 (Abstract) 1994
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

1: Am J Clin Pathol. 1994 Aug;102(2):223-30.

Flow-cytochemical differential leukocyte analysis with quantitation of neutrophil left shift. An evaluation of the Cobas-Helios analyzer.

Bentley SA, Johnson TS, Sohier CH, Bishop CA.

Department of Pathology, University of North Carolina School of Medicine, Chapel Hill 27514.

The Cobas-Helios (Roche Diagnostic Systems, Inc., Branchburg, NJ) is a new fully automated hematology analyzer that performs a complete blood count a differential leukocyte count (DLC), classifying leukocytes by flow-cytochemical technology. The DLC component of the Cobas-Helios was evaluated according to the National Committee for Clinical Laboratory Standards H20-A protocol. Instrument performance was acceptable with respect to all parameters investigated, including imprecision, inaccuracy and clinical sensitivity for the identification of quantitative and qualitative leukocyte abnormalities. In a minority of samples with neutrophil left shift, neutrophils tended to overlap the monocyte domain, resulting in overestimati of monocytes and underestimation of neutrophils. This problem did not affec clinical sensitivity and was generally associated with a positive instrumental left-shift flag. Flags for the identification of specific qualitative abnormalities of the leukocyte population (atypical lymphoid cells, nucleated red cells, blas cells, immature granulocytes and neutrophil left shift) performed well. In addition to a conventional five-part DLC, the Cobas-Helios also identifies an quantitates atypical lymphoid cells and "large immature cells," the latter corresponding to bands and immature granulocytes. Counts of atypical lymphoid cells and large immature cells correlated well with the equivalent c classes as enumerated by the reference method of the National Committee for Clinical Laboratory Standards. The Cobas-Helios offers the most reliable quantitative index of neutrophil left shift currently available in a commercial automated DLC analyzer.

PMID: 8042593 [PubMed - indexed for MEDLINE]